

# Non-Gonococcal Infection

## [Chlamydia - Mycoplasma]

### ★ History - Terminology:

### □ Chlamydial infections:-

- Chlamydia trachomatis is an important agent in both males & females - most common agent → eliciting STDs

• First name was Chlamydozoa that was formed of 2 parts:

- Chlamys → = mantle or cover (covering matrix around the elementary bodies in the cells infected w/ chlamydia)
- Zoa → belong to protozoa.

### ★ Pathology of Chlamydial Infection:

- The nature of chlamydia:

- Considered as bacteria ID. the following:-

- They contain Cell wall. similar to that of Gram -ve bacteria
- They contain Both DNA, RNA, Ribosomes & metabolic enzymes
- multiply by binary fission and they are susceptible to the antimicrobials.

### ★ Classification:

→ according to affected Host : 2 species:

- ① Chlamydia trachomatis :- Cause infection in human
- ② Chlamydia psittaci :- Cause infection in Birds.



- Those 2 species differ from each other in inclusion bodies → they produce in the infected cells and their antibiotic sensitivity:- as follows:

- |   |  |
|---|--|
| <ul style="list-style-type: none"> <li>- Chlamydia <u>Trachomatis</u> produce <u>glycogen containing inclusion bodies</u> → so they are stained with iodine</li> <li>- they are susceptible to Sulphonamides</li> </ul> | <ul style="list-style-type: none"> <li>- Chlamydia <u>psittaci</u> produce <u>inclusion bodies</u> that contain no iodine, and they are</li> <li>- No sensitive to <u>sulphonamides</u></li> </ul> |
|---|--|

→ according to the affected system:- 15 serotypes  
3 groups

- |  |   |  |
|--|---|--|
| <p>① Serotypes A, B, B<sub>1</sub>, C</p> <ul style="list-style-type: none"> <li>- Responsible for The Hyperendemic Trachoma of The eye</li> </ul> | <p>② Serotype D-K</p> <ul style="list-style-type: none"> <li>- Responsible for The Mucosal Surface of genital tract</li> <li>- Relatively non invasive</li> </ul> | <p>③ Serotypes L<sub>1</sub>, L<sub>2</sub>, L<sub>3</sub></p> <ul style="list-style-type: none"> <li>- Responsible for the Lymphatic tissue infection of the genital tract → lymphogranuloma venereum</li> <li>- Relatively invasive</li> </ul> |
|--|---|--|

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## ④ Pathogenicity and growth Cycle in the Host cell:

- The organism passes by 2 Phases before and after invasion of the host cells as:-

### ① Extra Cellular phase: (Elementary body)

- infective phase
- start by attachment to the Host cell followed by its phagocytosis by the host cell.
- its Not Digested and undergo organization to the 2nd phase or the initial body.

- These 2 factors of enhanced phagocytosis and inhibited Digestion are → important Virulence factors



## ② Intracellular phase (Initial body) (Reticular body)

- This body uses the host cell molecules to produce chlamydial nucleic acids and proteins → Divides by Binary fission followed by 2nd organization to Form the elementary bodies

- Finally → the host cell Rupture → with Release of these elementary bodies to infect other host cells

- The whole cycle takes 48-72hr

## ★ Clinical picture of chlamydial inf

↳ Serotypes D-K → produce mucosal affection, mainly similar to gonorrhoea with some Difference That will be stressed upon mainly non-gonococcal urethritis and Reiter's Syndrome

- Serotypes L1, L2, L3 → produce Lymphatic affection and lymphogranuloma venereum

## ⊕ Difference Between Gonococcal, Non-gonococcal Urethritis

↳ non gonococcal • Long incubation period. That may Range from 1 week to 5 weeks or longer

• may be Asymptomatic or with Scanty urethral Discharge that may be Thick and purulent

• Finally :- there may be no symptoms apart from urethral itching

## ⊕ Reiter's Syndrome :-

• Triad of :- ① Urethritis ② Conjunctivitis ③ Arthritis  
↳ may be other mucocutaneous manifestations That vary from one to other.

• it's an episode of arthropathy occurring within 1 month of an episode of Urethritis or Cervicitis



## → Other less Common names of RS

- Sexually acquired reactive arthritis SARA
- Conjunctivo-urethral-synovial syndrome
- Venereal arthritis
- arthritis urethetica.
- Idiopathic bleborrhoeal arthritis

## → Etiology of Reiter's

- Unknown, may involve one or more of the following factors:-

### [1] Genetic Factors:

60-70% of pts w RS → +ve histocompatibility antigen HLA-B27

### [2] Infective Factors:

- 1-4% of cases with non-gonococcal urethritis NGU may followed by (RS)

- It may occur also after gonococcal infection

⊕ RS Following NGU → is totally different from arthritis that occur as a Result of Disseminated gonococcal infection D.t gonococcal urethritis (GU)

⊕ The Arthritis in RS is D.t abnormal immune Response to NGU

⊕ The Arthritis Gonococcal is Due to actual Dissemination of gonococci from Urethra to Joints.

### [3] Immunological Factors:

- most of pt w RS - High antichlamydial antibody titres.

## → Clinical picture of Reiter's

### ① Mucocutaneous Manifestations:

- Urethritis precedes the appearance of RS

- Mucocutaneous lesion:-

  - ↳ Painless erosive Dermatitis

  - ↳ Small ulcers on the glans penis in males or the vulva in females

leading to Formation of Circinate balanitis, Circinate Vulvitis.

  - ↳ Small erosions and ulcers on the tongue or oral mucosa.

- Cutaneous lesion:

  - ↳ Scaly erythematous psoriasiform patches mainly on palms-soles [keratoderma blenorrhagica]

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## ② Articular manifestations :

→ mainly :- Arthritis  
(Non-suppurative, occur within 1 months of urethritis)

→ First joint affected is Sacroiliac joint  
Leading to → Sacroileitis

→ The Knee Joints :-  
↳ pain ↳ Tenderness ↳ effusion

→ The small joints of fingers :-  
↳ Fusiform Dactylitis  
↳ Tenosynovitis  
↳ Sausage Digits

## ③ Ocular Manifestations :

→ mainly :- Conjunctivitis

→ Rarely :- iritis, Uveitis

## ④ Other Rare manifestations :

- CVS :- - Carditis  
- aortitis & thrombosis

• Neuro :- meningitis, encephalitis, neuritis <sup>49</sup>

• Systemic :- generalized lymphadenopathy  
thrombophlebitis  
Amyloidosis

• The Cause of Death: D.t aortitis & Amyloidosis

## → Laboratory investigations

• No specific Lab test For RS.

• Lab finding :-

→ ↑↑ ESR, CRP, Circulating immune Complex, Leukocytes.

• The Synovial fluid of affected joints :-  
Turbid

• Culture of fluid → -ve (sterile)

• It shows → specific Cellular Response to the antigens of the genital or enteric microbes

## → Treatment

1 - Antibiotics → according to culture and sensitivity of the possible infections



## 2 - NSAIDs →

- Very effective in ~~the~~ of Arthritis  
such as:- Indomethacin 50 mg/3 times daily.  
Oral steroid → not much effective

## 3 - Cytotoxic Drugs → (Methotrexate)

4 - Immunosuppressive Drugs → (Aza thioprine)  
effective in severe cases.

## ★ Laboratory Diagnosis of Chlamydial <sub>inf</sub>

### [A] Culture Techniques:

- 1- Specimen → obtained by scrapping of Urethra or Cervix by swabs to obtain epithelial cells
- 2- The chlamydia is obligate intracellular organisms so they are found in the scrapped material rather than the Discharge or Urine
- 3- The obtained specimens are → refrigerated and transported to the Laboratory within 2 hrs in a transport medium that contain:- Sucrose and antibiotics to

inhibit other organisms

4 - Then inoculated into Tissue Culture Cell monolayers that are treated by:- irradiation or antimetabolites → to inhibit Cell Division in those tissue Culture.

5 - This induces the formation of giant cells that allows the growth of chlamydia inside their abundant cytoplasm

6 - Example of those tissue cultures:-  
- McCoy Cells treated with Cycloheximide.

7 - After 48 hr → The Culture is examined after staining with Iodine stain, Giemsa's stain or immunofluorescence stain to Detect intracellular chlamydia Inclusion bodies.



## 8 - Disadvantages of the culture

- Sure Diagnostic Tests
- Indicated before therapy to detect antibiotic sensitivity of the organism and after therapy as a test of cure

## B Non-Culture Techniques:-

### 1. Gene Detection:-

- PCR - LCR techniques.
- Advantages:
  - ↳ not invasive as the specimen is the Urine sample
  - ↳ sensitive and specific
  - ↳ very good Screening Tests specially in asymptomatic pts

### 2. Antigen Detection:-

#### • ELISA:-

- depends on detection of chlamydia antigen in the sample by adsorbing

it to polystyrene beads coupled to chlamydia monoclonal antibodies.

- This adsorption is detected in Spectrophotometer.
- This Test named as **Chlamydiazyme**.
- has good correlation with the Result of the Culture.
- more available, Less expensive

#### • Immunofluorescence test (MicroTrak test):-

- Detect:- chlamydia antigen by use of specific monoclonal antibodies to chlamydia conjugated with fluorescence.
- The advantages of Both Tests that they are sensitive and specific for screening But
- The Disadvantages are that they are Not recommended as test-of-cure because the antigens may persist despite killing of organism

### 3. Antibodies detection:-

- The Serological tests → Done by Micro-Immuno Fluorescence OR Complement Fixation. to detect antichlamydial antibodies.



## ★ Treatment of chlamydial inf.

### A Difficulties in treating chlamydia as compared to Gonococci:

#### 1- Compliance of the pt:-

- treated effectively by a single Dose whereas chlamydia usually needs multiple Doses a factor that ~~↓~~ the pt's Compliance.

#### 2- Cure rate:-

- may reach up to 95% → for gonococcal infections
- 80% → in non-gonococcal infection

#### 3- Culture:-

- The Culture of chlamydia are expensive
- Time Consuming
- Not always available.
- They are the only sure test of cure

### B Treatment Recommendations :-

#### ★ First choice regimens:

- Azithromycin 1gm single Dose orally
- Doxycycline 100 mg orally Twice daily for at least 7 days
- Tetracycline hydrochloride 500 mg orally 4 Times daily for 7 days.

#### ★ Alternative Regimens: [if others are contraindicated or intolerated]

- Erythromycin 500 mg orally 4 times daily / 7 days
- Ofloxacin 400 mg orally twice daily / 7 days
- Erythromycin → safe in pregnant women

### C Treatment Details:-

#### 1- Azithromycin:-

- azalide macrolide antibiotic
- used as a single (1gm) Dose orally or divided into 500 mg in the first day 500 mg in the 2nd day.
- High Cure rate For Both → gonorrhoea
- S/E → gastric Troubles → chlamydia



## 2 - Tetracyclines :-

- active against chlamydia
- Not giving with milk or milk products that inhibit their activity
- Contraindicated → pregnancy - children
- Some strains of chlamydia show partial resistance to this group.

## 3 - Macrolides :-

- Erythromycin → effective as tetracycline against chlamydia  
→ inactive against Mycoplasma hominis.
- safe in pregnancy

## 4 - Quinolones :-

- The best of this group: Ofloxacin

## 5 - Other Antibiotics :-

- \* The following antibiotics NOT indicated for the of chlamydial infections: Due to:

## - Penicillins groups :-

→ effective against chlamydia in vitro only  
But clinically the effective dose should exceed 30 million units of penicillin/per/day  
So they are not used

## - Rifampicin :-

→ effective against chlamydia in vitro  
But clinically there is rapid development of resistance to it. → So not used.

## - Aminoglycosides - Cephalosporins.

→ ineffective against chlamydia.



# 2 Mycoplasma infections :-

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## ★ 3 main groups :-

- ↳ Ureaplasma Urealyticum
- ↳ Mycoplasma hominis
- ↳ Mycoplasma genitalium

## ★ They are :-

- normal inhabitants of the urogenital tract in
  - ↳ males
  - ↳ females
- may have pathogenic Role in Urogenital infections

## ★ Clinical manifestations:

### [A] manifestations in the Males :-

#### 1- Urethritis :-

- Some Cases of non-gonococcal Urethritis

are Caused by : Mycoplasma hominis  
+ Ureaplasma Urealyticum

## 2- Epididymitis :-

- evidence That some Cases of epididymitis are Caused by : Ureaplasma , proved by : epididymal aspiration

### [B] manifestations in the Females :-

#### Bacterial Vaginosis

- offensive homogenous non-pruritic grey discharge
- absence of inflammatory changes in the vaginal wall.

That's way bacterial Vaginosis  
Replace "non specific vaginitis"

#### Pelvic inflammatory Disease

- Caused by : Ureaplasma Urealyticum and Mycoplasma hominis

### [C] manifestations in Male & Females :-

- Mycoplasmal infections in Both sex → may followed by Reiter's Syndrome



## Clinical manifestations in Infants:-

- Pneumonia
- Fever
- RDS

## Laboratory Diagnosis

### ① Culture:-

- Not Recommended as a routine test
- The Diagnosis Depends mainly on Clinical picture
- The main indications for Culture → in cases of persistent non-gonococcal urethritis that are -ve for chlamydia in order to do antimicrobial sensitivity test to direct the therapy

### ② The Swabs → streaked into mycoplasma/ureaplasma selective medium

→ Contain  
agar base  
yeast horse serum  
manganese sulphate  
urea, ampicillin

- They are incubated anaerobically for 48 hr at 37°C.

- Mycoplasma produces large colonies (50-500 mm in Diameter) with the ch. ch. fried egg appearance

- Ureaplasma → produces tiny colonies (50-100 mm) with the ch. ch. Brown colour D.t. → its ability to Utilize Urea

### ③ Treatment:

#### 1. Tetracyclines:

- effective against Both  $\left\{ \begin{array}{l} \text{Chlamydia} \\ \text{mycoplasma} \end{array} \right.$
- Some Resistant strains of ureaplasma → Reported
- This Resistance Caused by :- The same plasmid that codes for resistance of the gonococci to tetracycline

#### 2. Erythromycin:

- alternative to tetracycline in cases of :-  
↳ Resistance      ↳ pregnancy

60 - The Dose = chlamydia



# Lymphogranuloma Venerum

## ★ Terminology:

- Systemic Disease Caused by Sexual Contact
- Affect mainly the lymphatic system
- Caused by → Chlamydia Trachomatis Serotypes (L1, L2, L3) that have Tendency for invasive lymphatic affection
- Other name → Esthiomene → means Decay or Destruction occur in Vulva in Late stages.
- Other rare names :-
  - ↳ Tropical bubo, Frei's Disease, fourth venereal Disease, Nicolas-Fave Lymphogranuloma inguinale.

The transient, painless nature and the hidden site of the Ulcer in females (post-vag wall) → Cause late complications

## ★ Clinical picture:

### (A) Primary Stage :-

→ after IP (1 week - 4 weeks) → There may be a small ulcer → That may be on the Coronal Sulcus or intra-Urethral → in males  
- Urethral Discharge, post-wall of vagina or Cervix → in female

→ Occur in :- Rectum in 
 ↗ Females  
 ↘ homosexual males
   
↳ proctitis, tenesmus, Discharge, Bleeding from Rectum.

↳ The Ulcer → small, transient,  
↳ associated w/ Lymphangitis, Swelling of genital organs

↳ Heal → spontaneously



## B Secondary stage:-

- Start (1 wk - 4 wks) after Disappearance of the Primary Lesion
- Include The Following :-

### Inguinal manif

- painful tender enlargement of inguinal L.N on one or Both sides → **inguinal bubos**
- The enlarged inguinal L.N formed **2 groups** of swelling above, and, Below the inguinal ligament → that forms groove Between the 2 groups of swelling → **groove's sign**
- Finally → L.N fluctuate → Discharge of yellow purulent material with **ulceration** of overlying **skin**

### Systemic manif

- ↳ Fever
- ↳ headache
- ↳ Arthralgia
- ↳ in sever neglected Cases :
  - ↳ encephalitis
  - ↳ meningitis
  - ↳ hepatitis
  - ↳ Skin Rash:-
    - Erythema Nodosum
    - Erythema multiforme

## C Tertiary Stage:-

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### Anorectal manif

- prolonged Lymphatic Obstructions and granulomatous invol of rectal-mucosa

↓  
end in Rectal Stricture ,  
perirectal fistulae in females and homosexual males

- Occur in plns e-  
HIV infection Due to →  
Reactivation of the Disease

### Genital manif

- prolonged Lymphatic Obstruction → give rise to → genital Elephantiasis

with → excessive Destruction of the genital organs →  
esthiomene in females  
Saxophone in males

- There may be elephantiasis in Lower limbs



## ★ Causes of Death in lymphogranuloma venereum

1 - neglected late cases (main cause) include → gut perforation with peritonitis

Due to :- anorectal strictures

OR Destruction of its wall.

2 - Carcinoma → may Develop on top of long standing cases of genital elephantiasis OR rectal fistula and stricture.

## ★ Lab Diagnosis :- ch. 5

## ★ Treatment: [A] Recommendations:-

### ① First choice Regimens:

- Tetracycline hydrochloride 500 mg orally 4 Times Daily for 14 days
- Doxycycline 100 mg orally twice Daily for 14 Days

## ② Alternative Regimens:

(if Tetracycline are poorly tolerated.)

- Erythromycin 500 mg orally 4 times Daily for 14 Days

- Sulphamethoxazole 1 gm orally twice Daily for 14 Days

## [B] Treatment Details:-

→ Fluctuating inguinal lymph nodes → Aspirated by the use of a wide bore needle inserted into a healthy area of skin away from the L.N.

→ if they are incised and Drained There will be prolonged Discharge

→ • Delayed healing

→ perirectal, rectovaginal fistula and strictures → should Surgically Corrected

→ Suspicious areas → should excised

[63] and subjected to pathological examination to exclude → Carcinoma in Long standing cases



# Granuloma Inguinale

## ★ Terminology:

- Chronic Destructive Disease of the genital organs and adjacent areas
- it was known in the past **Donovanosis**
- The causative organism

Calymmato-  
Bacterium  
granulomatosis

→ The granulomatous ulcer → spreads in a serpiginous manner to the adjacent inguinal folds → to form indurated inguinal masses = **pseudobubos**  
that's because → The inguinal L.N not enlarged  
So there is No actual bubos

→ Scarring occurs in → chronic Cases with excessive formation of mutilating fibrous tissue that may spread along large areas of the genital organs, inguinal regions, the lower abdomen, thigh → forming extensive granuloma en cuirasse

## ★ Clinical picture:

### (A) manifestations of G. Inguinale:

- after IP (9-90 Days) the primary lesions:
- painless pepule OR nodule on genital organs in Both males & females

→ The lesion rapidly produce → Ulcer with granulomatous Base, rolled edges

### (B) Complications:-

- 2ry bacterial infection → in neglected Cases with fusiform bacilli →



Formation of Large painful Foul smelling  
Destructive (phagedenic) Ulcers on the  
genitalia with stenosis of the Urethral,  
vaginal & anal orifices.

- The Chronic ulcerative granuloma of  
the external genitalia (that characterizes the  
granuloma inguinale and other Tropical Diseases)

↳ maybe Risk Factors for spread of  
HIV infection

- Finally D.t. → the prolonged Ulceration  
→ 2ry infection  
→ Irritation  
→ Sq. Cell Carcinoma on  
Top of long standing Cases

## ★ Laboratory Diagnosis:-

↔ Introduction:-

- Causative organism:- Calymmatobacterium  
granulomatis  
↳ gram -ve bacillus → Can't cultured

on artificial media.

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- So the main method of Diagnosis  
depends upon

↳ Demonstration of organism in  
The Scrapping

↳ Biopsy from lesion.

- Biopsy from lesion is important →  
To exclude Carcinoma → in Long-  
standing Cases.

- The Diagnosis has 2 aims:

↳ Demonstration of the organism  
↳ Exclusion of Carcinoma.

## A Demonstration of Organism

★ Technique:-

- Scrapping from the lesion
- Better → small piece from the edge  
of the lesion → Crushed and.

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spread Between 2 slides

- The Resultant from smear is → air-dried heat fixed, stained with Giemsa stain eosin stain, thiazin, Wright stain

### the organism :-

- Calymmatobacterium granulomatis is → gram -ve → non sporing Capulated Bacillus
- Seen: Inside intracytoplasmic vacuoles of the histiocytes OR polymorph nuclear leukocytes.
- multiplies by: Binary Fission till production of about 20 organisms inside the vacuole.
- the organism stain :- Blue, Black with Wright stain → appear to have bipolar staining as its 2 poles → giving it a (safety-pin) appearance.
- The capsules stains :- pink around it



## B Exclusion of Carcinoma :-

- Histology show :-

- wide spread acanthosis
- Dermal infiltrations with plasma cells and histiocytes, few polymorphs with the organism inside their vacuoles.
- the edge → epithelial proliferation that should be differentiated from malignant change

### Treatment :-

#### ① Conventional Therapy :-

α. Tetracycline hydrochloride 500 mg 4 times daily for 3 weeks

α. Sulphamethoxazole - Trimethoprim Formed & 800 mg, 160 mg respectively

#### ② Recent therapy :-

- Norfloxacin - Azithromycin

- INH → G. inguinale → fail to Response.



# Chancroid

## ★ Terminology :-

- STDs → ch. ch By genital Ulceration
- in past → was considered the same as Syphilitic chancre.
- But it's a Distinct Disease Caused by Gram -ve bacillus "Haemophilus Ducreyi"
- Other names: Soff, sore, soft chancre  
↳ Ulcus molle

## ③ Tropical STDs :

## ⑤ Classic STDs

- ↳ The 3 tropicals
- ↳ Syphilis
- ↳ gonorrhoea.

- ↳ lymphogranuloma venerum
- ↳ granuloma inguinale
- ↳ Chancroid

## ★ Clinical picture :-

### ① Manifestations :-

#### 1- Chancroid ulcer:-

- after IP (1 week - 3 weeks) (usually < 1 wk)
- ↳ The ulcer begins as a transient papule that rapidly breaks into a painful ulcer :- with the following ch. ch :

#### ● Inspection :

- ↳ number : single , multiple
- kissing ulcers on 2 opposing surfaces on the under surface of the prepuce and glans penis

#### ↳ Site :

- mucous surface of prepuce
- Coronal sulcus
- Urethra in the males
- The frenulum

- labia majora , the Fourchette , clitoris
- the Urethra in females



- ↳ Size: 2mm to 2cm
- ↳ Shape: Irregular or Serpiginous
- ↳ Edge: Undetermined
- ↳ Floor: (seen Not felt)  
Covered w<sup>th</sup> granulation tissue or purulent exudate

### • palpation:

- ↳ Tenderness: - ptn feel pain on Pressure on the lesion. Ulcer tender
- ↳ Base:  
examiner puts his Thumb and index finger around the edge of the Ulcer and try to approximate them.  
- The Ulcer is soft

### ↳ Fixation:

- examiner puts his thumb and index finger around the edges of the Ulcer and tries to move the whole ulcer over the underlying tissue.

- The ulcer is Not fixed  
(Can be moved over the tissue)

## 2- Genital Discharge:

- purulent Urethral Discharge occur in cases with intraUrethral lesions
- Chancroid has to be differentiated from other causes of genital ulcers as well as other cause of genital Discharge

## 3- Regional L.N:

### • Inspection:

- ↳ Number: - multiple
- ↳ Site: - Inguinal group of L.N
- ↳ Side: - Unilateral in 50% of ptns
- ↳ Size: - Large size
- ↳ Shape: - Irregular masses (bubos) D<sup>t</sup> Peradenitis
- ↳ Surface:  
Overlying skin may be Red or Break with Suppuration after (1-2) weeks and formation of Sinuses.

### • Palpation:

- ↳ Tenderness: - Very Tender
- ↳ Consistency: - The L.N are either soft or show fluctuation when pus is formed
- Fluctuation is wave-like motion produced by palpation
- Body swelling when it contains fluid



↳ Fixation :- L.N fixed to each other as well as overlying skin.

## (B) Complications :-

- Stenosis of the prepuce (phimosis)
- Difficulty in its retraction (paraphimosis)
- 2ry Bacterial infection with fusiform bacilli → Destructive phagedenic ulceration that led in the past to
  - Destruction of the glans penis
  - gangrene
  - urethral stricture
- The genital ulceration in Chancroid →  
↑↑ The spread of HIV infection specially in Africa.

## ★ Laboratory Diagnosis :-

### • Introduction:

- The causative organism is *H. ducreyi*
- Gram -ve bacillus That needs to be cultured on Blood enriched media.

- The Diagnosis depends on:-

• Demonstration of the organism mainly use → Blood Culture (rather than smear that is not reliable)

- The Diagnosis has 2 aims :-

- ↳ Demonstration of organism
- ↳ exclusion of other causes of genital ulcers

## [A] Demonstration of the Organism :-

### • The techniques:

- Tissue taken from the edge of the ulcer or from aspiration of the bubos
- 1- Smear stained with Giemsa stain, wright stain, Gram stain
- 2- The Culture is more reliable.
  - It's grown on Blood-enriched gonococcal agar Base OR Mueller-Hinton agar Base
  - Culture media → incubated at 33°C in environment with 100% humidity and CO<sub>2</sub>.



- within 48 hrs → The Colonies appear as yellow-gray Dome Shaped 1 mm in Diameter → adhesive when touched with a wire.

3 - Recently → Chaneroid Can Diagnosed By PCR (more sensitive & more specific)

### ● The Organism:-

- small gram -ve Bacilli with Rounded ends
- appear in groups or rows Containing about 20 organisms giving appearance [School of fish or railroad tracks]

### ● Histopathology:-

- The Biopsy show:- 3 distinctive Zones
- 1- patchy necrosis of the epidermis with occasional acanthosis and Neutrophils in the superficial Zone
- 2- proliferation of the Endothelium

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of The Blood vessels in mid Zone  
3- plasma cells and lymphocytes infiltration in the Deep Zone

### [B] Exclusion of other Causes of Genital Ulcers

- Differentiated from other Causes of genital ulcerations Including:

- \* Chancre : by darkground microscopy
- \* Granuloma inguinale : has some similarity
- \* Herpes progenitalis

### (★) Treatment:-

#### ● Introduction:-

- liable to produce antibiotic resistance.
- this resistance is an extra-chromosomal or plasmid mediated.

↳ Those plasmids are similar to the plasmids of N. gonorrhoea.



- They can mediate Resistance against:
- Ampicillin - tetracycline - Sulphonamides
  - Trimethoprim

→ So: proper antibiotic Sensitivity Testing.

- adequate tx

- prolonged follow up

is essential → to ensure the Cure.

→ Being one of the Ulcerative STDs ∴  
most important to test for HIV  
at the initial visit and after 3 months.

### Single Dose Regimen

- Azithromycin 1gm orally
- Ceftriaxone 250mg I.M

### Multiple Dose Regimen

- Erythromycin 500mg orally / 4 times / for 1 wk
- Ciprofloxacin 500mg orally / twice / for 3 days
- Amoxicillin 500mg combined w/ Clavulanic acid 125mg / orally / 4 times / 3 days

⑥ The enlarged Fluctuating inguinal L.N (bubos) → should never be incised

↳ as the healing is very Slow

⑦ They should be Aspirated by a wide pore needle through healthy area of skin away from the bubos



# Syphilis

## \* Terminology - History :- Future:

- D.F :- prenatal or acquired systemic infection.
- organism :- Treponema pallidum
- site :- occur at any tissue or vascular organ
- Names :- many names and many victims :-

↳ Christopher Columbus

↳ who accidentally acquired the disease and transmitted it on his return to Europe to start the epidemic of this New Disease in Europe.

The king and queen of Spain:

↳ Received him at that time with the highest honours for his discovery of the new world.

Surgeon John Hunter:

↳ acquired the disease by self-inoculation of venereal discharge of a ptn → unfortunately this ptn had syphilis and gonorrhoea at the same time who at past considered one disease.

- All Deaths Due to Syphilitic Heart Disease.

• Other names :- Lues = pestilence or plague (which given to any contagious malignant epidemic D)

great pox :- as opposed to small pox which was considered at that time relatively mild epidemic

great imitator :-

• Sir William Osler says :-

"known syphilis in all its manifestations and relations and all other things clinical will be added into it"

• The primary lesion of syphilis "Chancre" means in latin "Cancer"

↳ The actual link Between syphilis and Cancer → leukoplakia of the tongue → occur interitery stage → predispose to Carcinoma of tongue

• Future :-

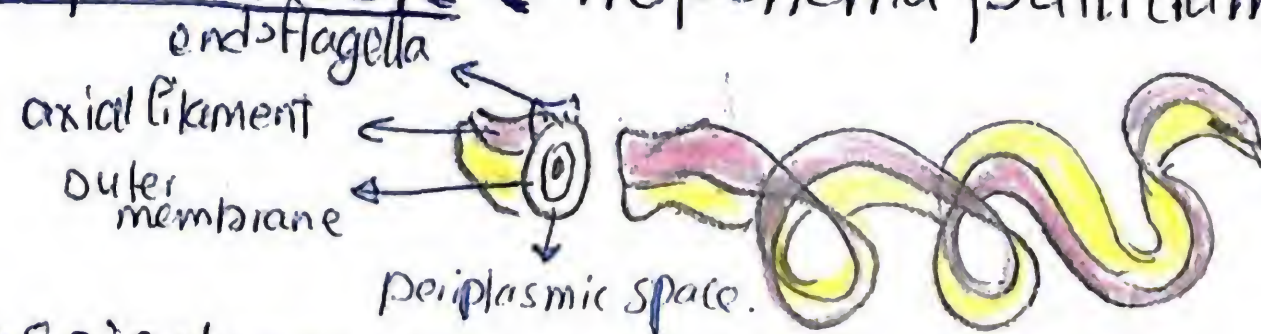
→ after availability of Penicillin therapy → the false sense of security from syphilis

↳ The situation changed dramatically with appearance of HIV inf. the new plague of 20th Century



## ★ Causative Organism:-

### • Spirochaete (Treponema pallidum)



→ Spinal organism of (6-12) regular coils with length of (6-12  $\mu$ m) width (0.12-0.25  $\mu$ m)

→ show 2 Types of motility :-

1. Locomotion :- informal Corkscrew or propulsive movements
2. Change in shape in the form of :- angulation, elongation undulation

→ The tiny size of the organism renders it below the level of resolution of conventional light microscopy and hence the Darkground microscope → should be used to observe it and its motility Directly.

→ It can be stained by silver or immuno-fluorescence stains though they are not used practically.

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## • Other Spirochaetes :-

- Borrelia refringens • B. balanitidis should Differentiated from T. pallidum
- Trepanema that cause pinta, yaws (T. Caraleum, T. pertenu)
- T. microdentum or T. macrodentum that are responsible for Dental Caries Found in oral cavity
- non-pathological Rieter strain
- Nicol pathological strains

## ★ pathology:-

### A} Early phase :-

- Organism enter the body through abrasion in skin or M.M → Local tissue Reaction of two 2 components:

1. Cellular infiltration with plasma cells and lymphocytes
2. Vascular reaction :- Endarteritis



obliterans (Thick, Hypertrophic intima)

- The organism Reach the Regional L.Ns leading to → Lymphadenopathy followed by → invasion of Blood stream.

### B<sup>3</sup> Late phase:-

- There is Balanced state Between Trepanoma that give No symptoms and antibodies in the Serum
- If this balance is Disturbed → late manifestations occur → in form of gumma show the same tissue Reaction
  - + - Necrosis
  - Vascular or neurological affection.

## ★ Classification:

(A) Acquired Syphilis : Divided acc. to time

### ● Early phase:

- During the first 2 yrs

- The ptn is infective to others.

- It includes:-

Primary stage

- One month
- Occur after incubation period of 9-90 days
- manifested by:

Chancere

2<sup>nd</sup> stage

- Two months
  - manifested by:
- Generalized affection

• Both stages:-  
Asymptomatic

- Early latent Syphilis

↳ means that the ptn is still within the first 2 years of infection

↳ because the ptn is Asymptomatic.

### ● Late phase:-

- Occur after the first 2 yrs of infection.

- The ptn is Not infective to others

- It includes:

↳ Late Latent Syphilis:-

↳ ptn has passed the first 2 yrs of infection

↳ ptn is Asymptomatic



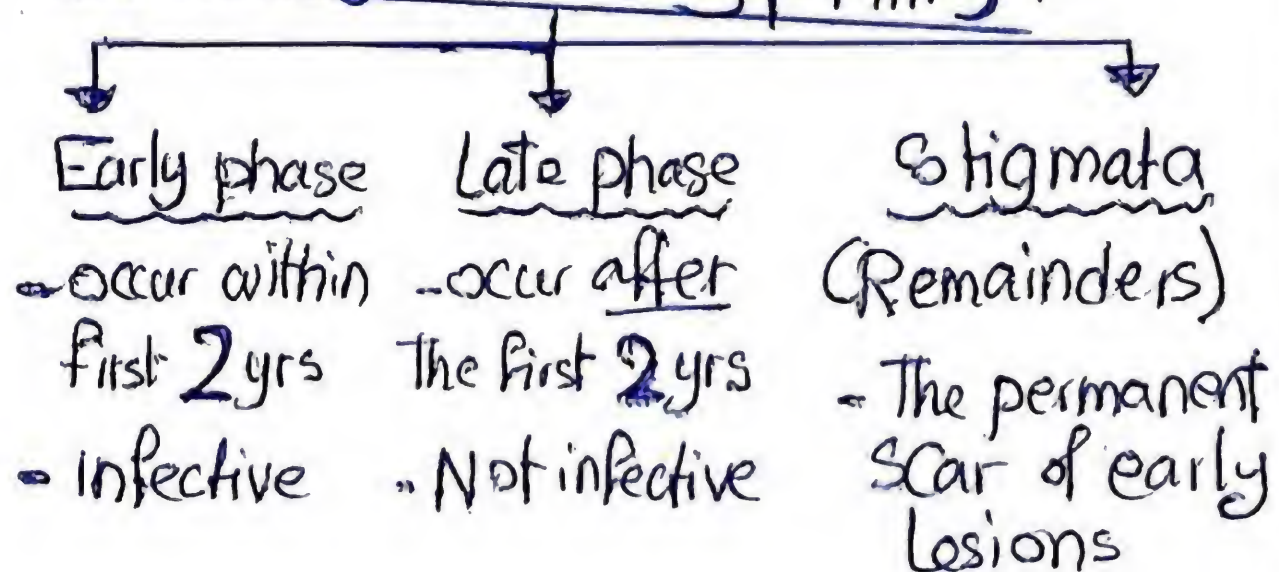
## → Tertiary stage:

- This stage after 3 or more yrs +
- main manifestation is **Gumma**

## → Quaternary stage:

- occur after 20 or more years
- the main manifestations are **CVS** and neurosyphilis
- Both stage are **Asymptomatic**.

## (B) Congenital Syphilis:



# Primary Syphilis

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• after 1P (9-90 days) → the Chancere appears.

↓  
start by papule that gives painless ulcer  
with the following Criteria:

### (A) Inspection:

↳ number: Single → 1st local immunity

↳ Site:

- Genital → male → Coronal sulcus  
glans penis  
Frenulum  
(concealed) inside urethra  
meatus

Female → labia majora, labia minora  
meatus, Cervix (concealed)

Extragenital → Anus, lips, tongue, nipple, areola.

↳ Size: (0.5-2cm) in Diameter

↳ Shape: Rounded or oval

↳ Edge: Raised at periphery, slopping toward center

↳ Floor: (seen not felt) → clean, pale or red  
↳ oozing serous fluid



## ⑧ Palpation:-

↳ Base:- (felt not seen)

- Indurated :- if the lesion is held between index and thumb,
- They can't be approximated

↳ Tenderness:- Abscent

↳ Fixity:- not fixed to deeper structures (if the lesion is held between index and thumb → it can be moved)

↳ Fate:-

- Show healing without treatment in about 2 months with a thin scar

## ★ Variants of primary Syphilis:-

1- Chancre Redux:-

Chancre Develops on the scar of previously healed chancre.

2- The chancre painless - Not Tender :- Due to Degeneration

of nerve axons in the lesion

- it may be painful → if there is 2ry infection that is common in AIDs pts

3- ptne 1ry Syphilis who present Neither Chancre nor inguinal L.N:-

- occur in female & Chancre on the Cervix → So No lesions on the genitalia

- also :- the Cervix Drains to the deep iliac L.Ns  
So no inguinal nodes

## 4- pseudochancere Redux:-

• Its a Gumma → Develops on the Scar or healed chancre (Not treponema or L.N)

## ★ Inguinal L.Ns:-

- Bilateral - Symmetrical - painless Enlargement
- Rubbery in Consistency - freely mobile
- Not Tender - the overlying skin → Normal

- Some ptne may present by :- enlarged L.N with healed or abscent chancre (Bubon d'emblee)



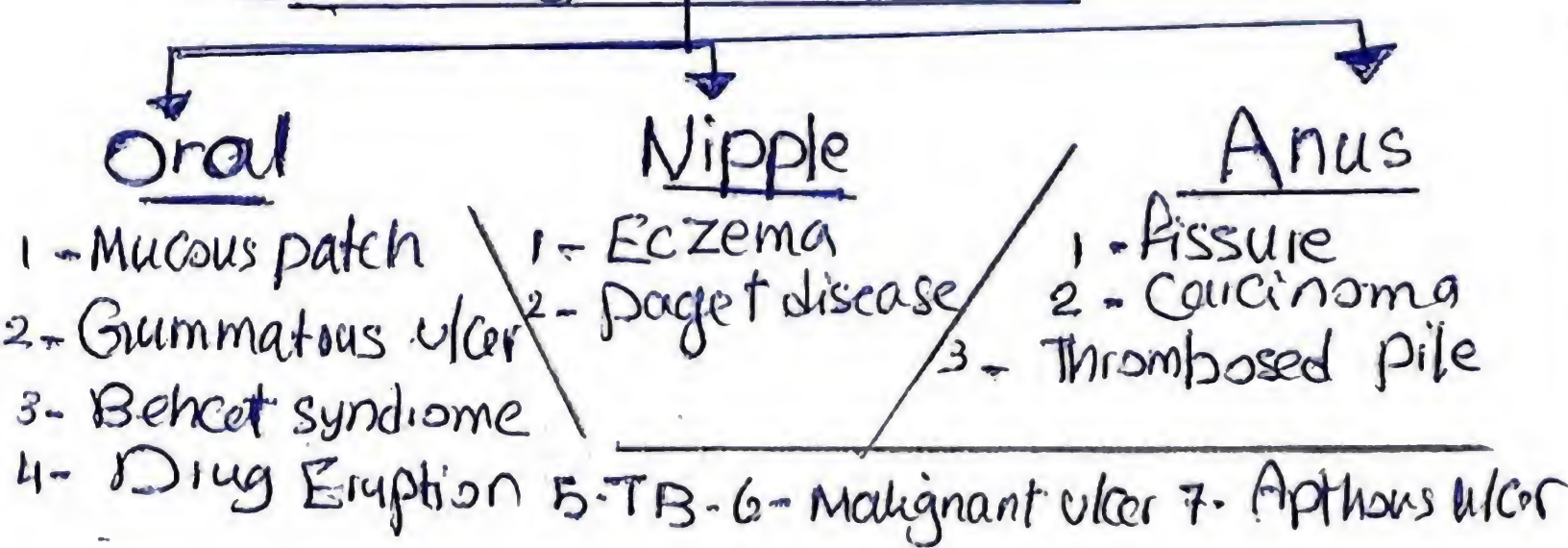
# ★ Differential Diagnosis :-

## [A] Genital Chancre :-



- |  |  |
|--|--|
| 1. Traumatic ulcer (scabies)<br>2. T.B ulcer<br>3. Herpes Zoster<br>4. Malignant ulcer<br>5. Ulcer of Drug Eruption<br>6. Bilharzial ulcer<br>7. Behcet syndrome | 1. Herpes progenitalis<br>2. Chancroid<br>3. Lymphgranuloma venereum<br>4. Granuloma Inguinale<br>5. Scabies<br>6. Primary HIV ulcers<br>7. Mucous patch ulceration of 2ry syphilis<br>Gummatous ulcers of Tertiary Syphilis |
|--|--|

## [B] Extragenital Chancre.



# ★ Diagnosis of 1ry syphilis 72

## [A] Darkground Microscopy

- The only Sure method for Diagnosis
- The idea :-
  - Depends on the Observation of the organism and its motility by making light rays diverge from the looking eye  $\Rightarrow$  Dark Background.

When these Divergent rays face the organism  $\rightarrow$  they deflected towards the eye.

- So the Organism appears Luminescent against Dark background and its motility can be examined.

(Done by  $\rightarrow$  change the diameter of the opening of the condenser to diameter of

## ★ the material for examin. :- (0.8 cm)

- From the ulcer or L.N

## ★ Exudate from the ulcer :-

the ulcer should be cleaned with gauze soaked in water OR Saline to remove Scabs. (not antiseptic  $\rightarrow$  kill the organism)



- This is important → to Remove Saprophytic organisms in Dirty genital lesions as :-  
[*Borrelia refringens*] [*B. balanitidis*]
- Sulphonamides given in a dose of 1 gm / 4 times / Day are useful to guard against Sepsis
- They have the advantage of being non-treponemoidal Drugs.

✱ Aspirate from L.N :- indicated in Cases with -ve results on ulcer exudate or there was antiseptic application on it or if it is hidden or healed.

(B) Serological Tests :-  
+ve Results in 50% of ptns.

## Secondary Syphilis

✱ General manifestations :-

- after period of about 8 weeks from the appearance of chancre,

50% of untreated ptns → Presented by :- 73

- Severe headache
- Fever • meningism

Due to early invasion of CNS  
- for the same reason → There may be Nerve Deafness

- Eyes :-  
→ Iritis → Choroidoretinitis

- Scalp :- Eye brows :-  
Irregular patches of alopecia → giving them the appearance of "moth eaten alopecia"

- Hepatitis • Splenomegaly :-  
- generalized Lymphadenopathy.  
Cervical, Occipital, axillary, epitrochlear.  
- Discrete, Rubbery, painless  
- Overlying skin = Normal

✱ Skin manifestation :-

1- Skin Rash :- Syphiloderm  
syphilids



- Bilateral, Symmetrical Maculopapular Rash

- generalized

- Show: Variable Scaling giving a psoriasiform appearance

- Coppery Red colour.

- Cause: Itching in some pts.

- Occur at anterior Hair line giving rise to (Corona veneris) OR hair line on the neck (collar of Venus)

- the most common sites:

→ palms → soles → papules surrounded by white Ring

- Important Clinical Red Flag for diagnosis of Syphilis

- there is Laboratory Red Flag in Diagnosis of Syphilis (in neurosyphilis)

- in the undernourished OR Immunocompromised Pts → The papules show:-

Central necrosis with pus formation → forming pustules with excessive crusts.

[Oyster Shell OR rupial Syphilis]

## 2. Mucous Patches <sup>74</sup>

- Start as papules that rapidly ulcerate.

- They appear as greyish white patches gives → sloughs → separate → leaving a serpiginous ulcer [snail track ulcer]

- They affect mainly:-

tonsils, tongue, angle of mouth, nose, larynx → hoarseness

## 3. Condyloma Lata

- the most infective lesion of syphilis

- Occur in moist skin areas:-

axilla, groin, under Breast, Perianal area.

- appear as: Large fleshy masses with rounded outline

- They have broad neck (sessile)

- Their surface shows: Necrosis with oozing of fluid that is full of Treponema.

- They have to be differentiated from Condyloma acuminata (venereal warts)



- that show skin colour, rough surface
- they are Dry lesions and pedunculated.

## ★ Diagnosis of 2ry syphilis:-

### 1- Dark ground microscopy:-

- The fluid is obtained from moist lesions such as Condyloma lata or mucous patches

### 2- Serological tests:-

- They give +ve results in 100% of ptms.

\*- HIV infected syphilitic ptms → abnormal Serologic test results either

- very High - very Low or - unusual fluctuating titers.

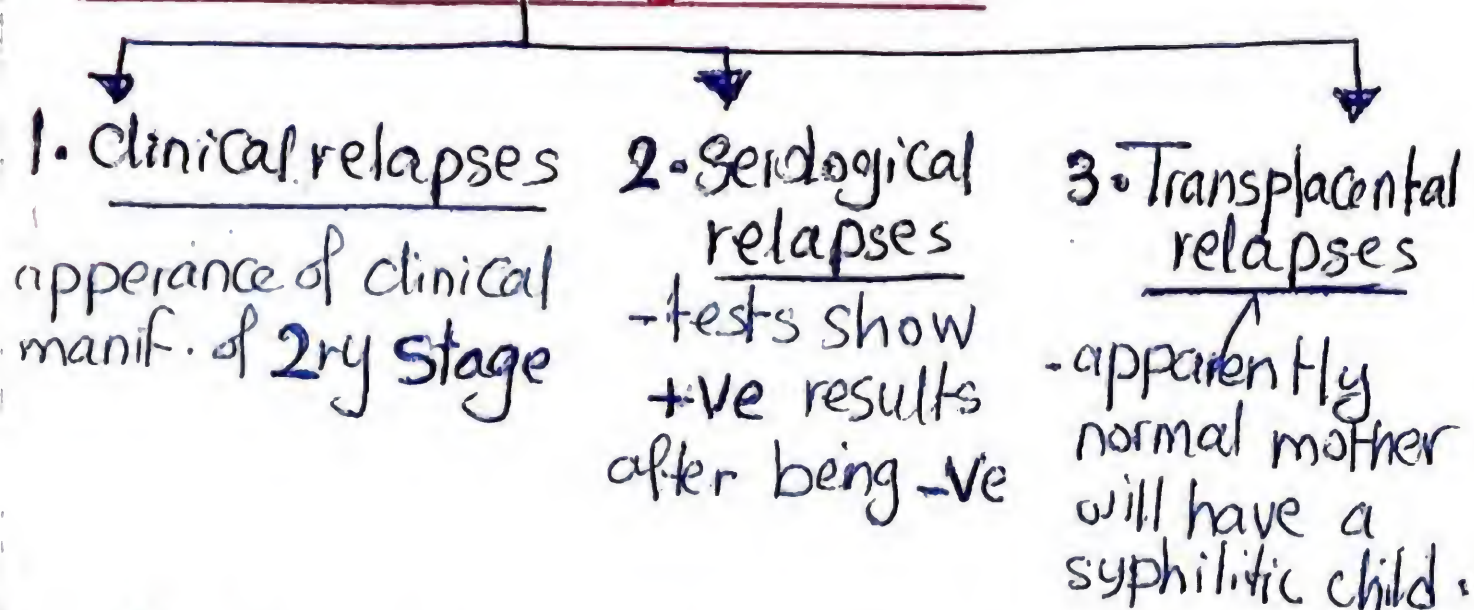
↳ For these ptms: Skin biopsy : alternative test

## Early Latent Syphilis:

### ◎ Ch. ch. by:-

1. Absence of clinical manifestations
2. +ve Serological tests: **VDRL**  
**TPHA**

## ◎ Relapses in early Syphilis:



## Late Latent Syphilis

1. This is non-infectious stage that occurs after the 2nd yr of infection and persists for years.
2. The ptm is discovered accidentally During performing the tests for blood donation or premarital tests as +ve Serological tests are the only findings.
3. The Danger in this State is Not the infection But the possibility of neurological or CVS complications
4. The following should be done:-  
↳ CSF examination → to exclude neurosyphilis



↳ X-ray and echocardiography :-  
to exclude syphilitic aortitis

↳ Re-examination of ptn with quantitative VDRL  
or RPR at 3, 6 months interval

- They are to be repeated every year for 3 years if they are still reactive

## Tertiary syphilis

### ★ Pathology :-

#### ↳ 1. Localized form :- (Gumma)

↳ Size :- Few millimeters to many centimeters

↳ Central necrosis surrounded by peripheral fibrous tissue.

↳ under microscope :- marked endarteritis obliterans (marked than early phase)

• marked necrosis  
(D + tissue Hypersensitivity)

↳ The cellular infiltrate formed :-

Plasma cells, lymphocytes, fibroblasts

with absent or scanty organisms

↳ Lymphadenopathy → Found in Early phase is Not found in this stage.

↳ Gumma → occur in Covering structures as Skin, S.C, Submucous Tissue  
→ occur in Supporting structures as Bone - muscle - joints - viscera

#### ↳ 2 Diffuse form :-

- Diffuse syphilitic Reaction in the Organ as in tongue or testis.

### ★ Clinical Picture

#### ① Gumma of Skin :-

- appear as single or grouped nodules that are Not symmetrical

- Nodule → Rounded, Red, freely mobile

- heal by :- thin scar OR pigmentation or may give Ulcer

- Gumma ulcer :- Clean surface, (Wash-leather)  
punched out edges.



## ② Gumma of S.C. tissue

- the lesion later become attached to the overlying skin and gives Ulcer with punched out edges and wash leather floor.
- The ulcer heal with :- thin atrophic non-contractile Scar (tissue paper scar)
- The main site are :- Lower leg  
Face - Buttocks

## ③ Gumma of Mucous membrane

- gives :- Ulcer → lead to perforation in the palate → Destruction in nasal septum or laryngeal stenosis
- Syphilis of tongue →
  - occur either in primary stage (chancre)
  - 2<sup>nd</sup> stage (mucous patches)
  - Tertiary stage in 2 forms
    - Localized (Gumma) → ulcerate
    - Diffuse interstitial fibrosis

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leading to → thickening of the tongue and glazed surface (atrophied papillae), fissuring leukoplakia (white thick plaque), S.C.C.

## ④ Gumma of Supporting Structure:

### A Bones:

#### ① Syphilitic periostitis (Long Bone):

- Cellular infiltration of :- plasma cells, lymphocytes, epithelioid cells, giant cells, Osteoblasts around the Blood vessels
- ↳ leads to :- Stimulation of new Bone under the periosteum with Rough irregular surface.
- This new Bone formation leads to: Thickening of the Bone. so No pathological fracture.
- It affects mainly: Tibia.

#### ② Syphilitic Osteomyelitis (Flat Bone):

- Cellular infiltration in medullary cavity
- No. sub-periosteal new Bone formation
- ↳ This renders Bone Destruction more likely to occur.



- It affects mainly → Skull vault → giving it worm-eaten appearance.

- The hard palate & Nasal septum may be affected.

### - Clinically:

- History of trauma followed by → Deeply seated pain (may be very severe) specially at night associated with :- Swelling of the Bone

• Perforation in palate → give rise to Difficult Breathing

### - Radiologically :-

- The long Bone show thickening of the Periosteum and opacity in medullary cavity. It → new Bone formation

- in the Tibia → apparent on its anterior part giving it a bow-like appearance. (sabre tibia)

- Skull show Osteoporosis

## B Cartilage :-

• Pericondritis in the ear, nasal septum, Costal cartilage, Destruction.

## C Viscera :-

### Liver

- multiple localized gummata
- with fibrous tissue formation
- Distortion of shape of liver without affect its function
- may affected by Diffuse fibrosis
- ↳ ends by: Liver Cirrhosis & disturbed liver function
- portal HTN
- Splenomegaly

### Stomach

- localized or diffuse gummatous reaction
- with dyspepsia similar to peptic Ulcer.
- Diagnosed by: Endoscopy Biopsy

### Testis

- localized or diffuse Reaction
- painless enlargement of testis
- Loss of sensation
- gumma may ulcerate Through scrotal skin giving: anterior scrotal Ulcer that different from Tuberculous Ulcer which found in: posterior surface of Scrotum due to Tuberculous affection of epididymis That is on The post aspect of testis.



# CVS Syphilis

## ★ Pathology :-

- occur in: - 10-15% of untreated pts
- after: 10-15 yrs Common in: males.

### A Syphilis of Heart

- ↳ may be Localized (gumma) which may affect the septum → Heart Block
- ↳ may be Diffuse → affect Myocardium leading to → Heart failure.

### B Syphilis of Medium vessels

- ↳ may Destroy the elastic layer of media → aneurysmal Dilation.
- ↳ Proliferation of intima → pathological narrowing.
- ↳ it affect → Cerebral vessels
  - ↳ Spinal
  - ↳ Carotid & iliac & femoral arteries

## C Syphilis of Great Vessels (Aorta)

1) ↳ the organism reaches the vessel through Vasa Vasorum in the adventitia → where it excites Cellular infiltration of plasma cells and lymphocytes with late fibrosis in the adventitia and narrow Vasa Vasorum

2) ↳ these changes lead to → fibrosis, Destruction of the media with stretching, aneurysm formation.

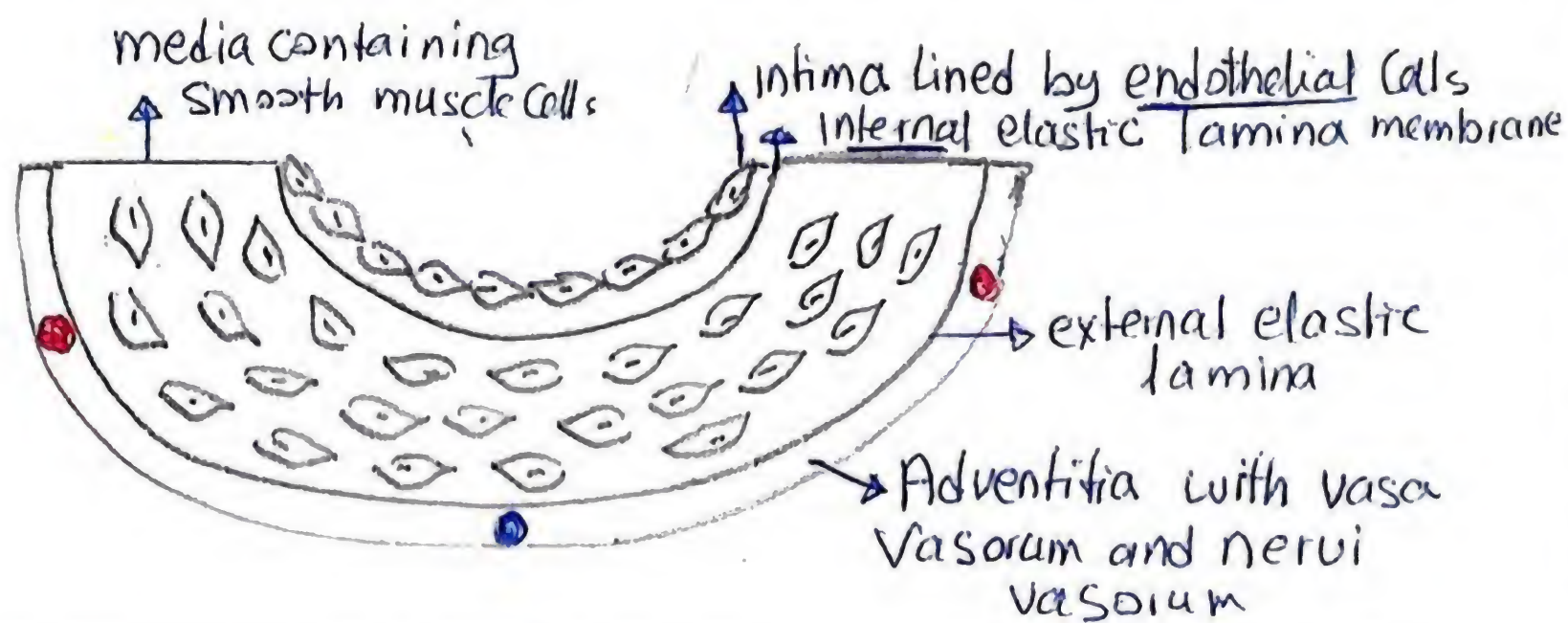
- (- Aneurysmal Dilation D/t atherosclerosis has fusiform appearance)
- (- if Dilation → extends into aortic ring → it leads to aortic incompetence)

3) ↳ these changes leads to → Distortion

- ↳ thickening
- ↳ Calcification patches on intima

- If extends to their openings at the root of aorta → leads to → Coronary ostial stenosis





## ★ Clinical picture :-

### Ⓐ Uncomplicated Aortitis :

- Few symptoms, signs
- lead to → retrosternal Dull aching pain  
Due to stretch of nerves in the sheath of artery

### Ⓑ Aortic Regurgitation :-

#### Symptoms

- \$ of left heart failure :-
- Dysnea on exertion or at night → complicated By- Heart failure of Right side with swelling in the abdomen and lower limbs + upper abd.

Pain - palpitation D't Hyperdynamic Circulation

#### Signs

- 1- Water hammer pulse :- D't High systolic pressure and Low Diastolic pressure at Radial artery
- 2- pistol shots :- D't the same Cause (at the femoral artery)
- 3- prominent Capillary Pulsation at the Skin & Nail Bed
- 4- Cardiac signs :
  - left ventricle enlargement
  - forcible Apex beat
  - aortic Diastolic murmur over aortic area
  - mid-Diastolic murmur heard over apex.

## Ⓒ Aortic Aneurysm :-

### 1- Ascending aorta :

- most common site
- Its Rupture lead to Sudden Death D't Cardiac tamponade.
- suspected by presence of parasternal dullness and aortic systolic murmur.

### 2- Arch of the aorta :-

- Pressure on :-

3 tubes	3 nerves	3 vessels	3 Bones
• Trachea ↓ Stridor	• left Recurrent laryngeal nerve ↓ Hoarseness	• Aortic Branch • azygous vein • Sup. vena. Cava.	• Ribs • Sternum • Vertebrae ↓ erosions + fracture
• Oesophagus ↓ Dysphagia	• phrenic N. ↓ Diaphragmatic paralysis		
• Thoracic Duct ↓ edema of Lower limb	• Sympathetic Chain → Horner \$		
		3- <u>Descending Aorta</u> - erosion - Lower Back pain	



## D Coronary Osteal Stenosis :-

- Anginal pain on exertion or at Rest (Angina of Lewis)
- Coronary thrombosis  $\rightarrow$  Sudden Death

## ★ Diagnosis :

1. Clinical picture
2. X-ray :-
  - linear Calcification of aorta
  - Left Ventricular enlargement
  - Aortic aneurysm
  - Erosion of ribs, Sternum, Vertebrae
3. ECG :-
  - Left axis Deviation
  - Arrhythmia
  - Elevated S-T segment
  - T-wave changes
4. Serological tests for syphilis = +ve

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# Neurosyphilis

## A Asymptomatic Neurosyphilis :

$\rightarrow$  No neurological manifest but CSF show changes:-

- Cell Count (Lymphocytes)  $> 5$  HPF
- Protein  $> 40$  mg/l.
- +ve Serological test for syphilis
- Colloidal gold test:-

$\rightarrow$  ratio of albumin to globulin in the CSF may show:- The predominance of globulin that precipitate colloidal gold over albumin that protect it from precipitation

$\rightarrow$  if these findings are present even in absence of symptoms and signs  $\rightarrow$  the pt may develop:- Symptomatic neurosyphilis [Red flag of Stokes]

## B Meningeal neurosyphilis :

### 1. Brain :-

#### ★ meninges of the Vertex :

- $\rightarrow$  Convulsions, aphasia, Confusion
- $\rightarrow$  headache, vomiting, papilledema



## ★ Meninges of the Base :-

↳ paralysis of Cranial nerves 3, 4, 6, 7, 8  
leads to Ocular, Facial, Auditory Complications

## ★ Ventricles :-

↳ Hydrocephalus  
↳ subependymal gliosis → Argyl Robertson Pupil

pinpoint irregular pupil  
Loss of light Reflex  
preserved accommodation reflex

(Ependyma :- membrane lining the Cerebral Ventricles and the Central canal of spinal cord)

Gliosis :- fibrosis of in the nervous tissue)

## 2- Spinal Cord :-

- The affection of Cervical Region leads to → Lower motor neuron lesion at the level of the Shoulder girdle

Upper motor neuron lesion Below The level of the Cervical region [Erb's Spastic paraplegia]

## [C] Vascular affection :-

- affection of Cerebral - Spinal vessels by [87] → thickening and adherence of the Dura

narrowing or thrombosis → Vascular Ischemia

- may be gliosis of different tissues & different neurologic manifestations :-

↳ Occlusion of ant spinal artery → paralysis of lower limbs & Urinary incontinence

↳ Occlusion of the post spinal artery → Sensory loss below the level of lesion.

## [D] Paralytic neurosyphilis :-

### ⊙ Localized affection (gumma)

- rare affection  
- gives → general manifestations of :-  
    ↑ Intracranial tension → headache  
                                    → Vomiting  
                                    → papilledema.  
+ specific manif. according to the involved area.

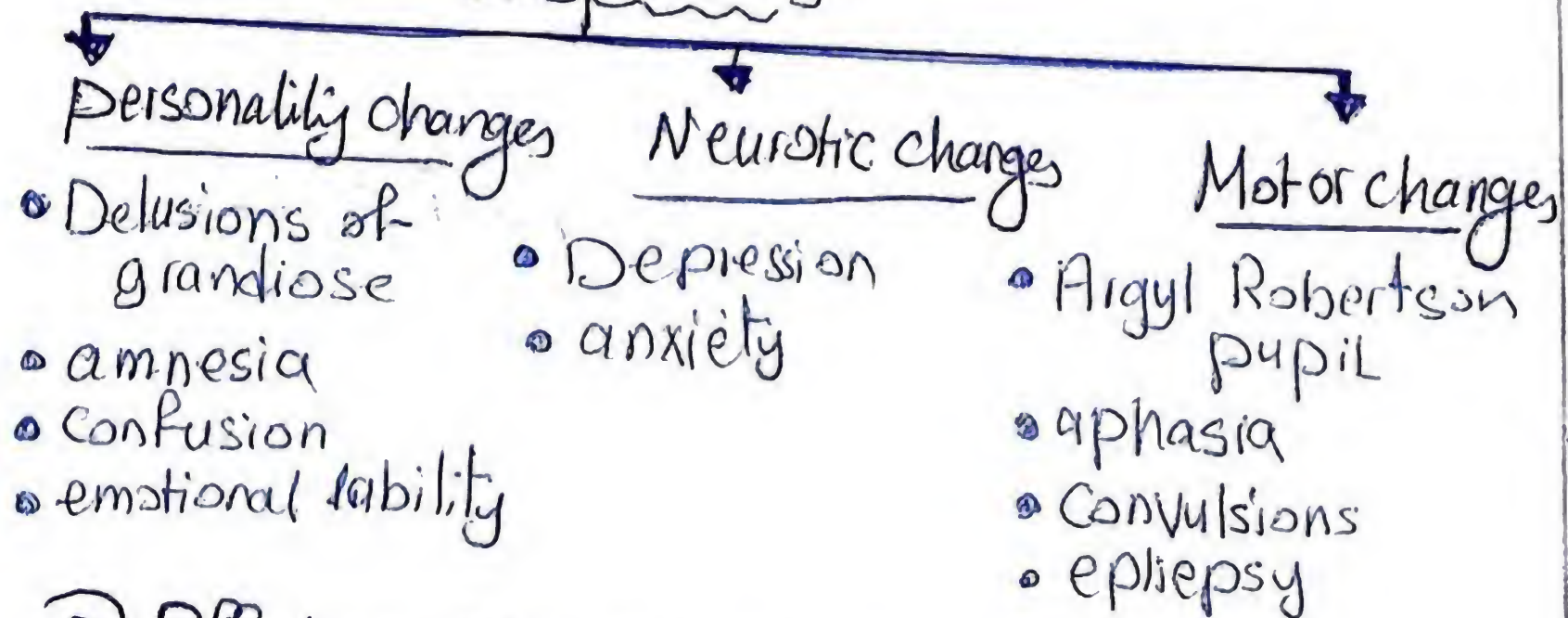
### ⊙ Affection of the Brain

→ lead to :- general paresis of insane  
- Diffuse infiltration of Cerebral Cortex



to the skull vault and atrophy

- gliosis of Cerebral cortex with dilated ventricles → manifested by:



## ① Affection of the Spinal Cord:-

→ leads to:- Tabes Dorsalis

→ Diffuse infiltration of the spinal cord → degeneration of lumbosacral Region mainly:-  
in posterior roots of Post. Column,  
Posterior ganglia

→ the following manifestations:-

1- Progressive loss of vision D.t:- optic nerve atrophy

2- Tabetic Crisis:- there is sudden attacks of  
acute abdomen, renal colic, tenesmus,  
Laryngeal stenosis → Stridor

3- Urinary - Rectal Troubles as:-  
Incontinence of urine & stools

4- sensory ataxia: D.t → Loss of  
Proprioceptive sensations (sense of position)

5- Paresthesia in the Legs

6- Lightening pains:- Intermittent attacks  
of severe pain in the legs.

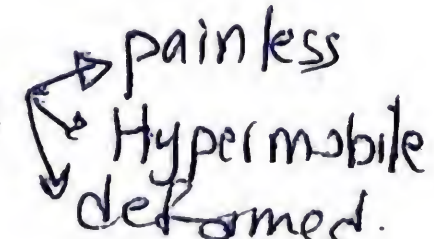
7- Trophic changes:- Result from: Loss of nerve  
supply.  
manifest by:

- Skin:- perforating ulcer in sole of foot

- Joints:- Charcot joint → painless

Hypermobile joint → ends by degenerative  
changes D.t repeated Trauma.

- affect Knee joint

- Clinically: the joint is   
painless  
Hypermobile  
deformed.

- Radiologically:

- joints show Erosion - Destruction  
of Cartilage - Osteophytic growths

- Sclerosis of bony ends.



# Congenital Syphilis

## (A) Introduction:

[A] *T. pallidum* in maternal circulation → pass through placenta after the 4<sup>th</sup> month of pregnancy to the foetal circulation

→ which produce the following effects in the successive pregnancies according to:

[Kassowitz law]

- Abortion after 4<sup>th</sup> month of pregnancy
- Premature baby
- Stillborn baby
- Liveborn baby will develop signs of syphilis
- Liveborn baby will remain healthy.

→ There is Better prognosis with successive pregnancies 1<sup>st</sup> → Prolongation of the period from the Date of the infection of the mother.

[B] Baby may be healthy at Birth But may develop syphilis after weeks or months one should depends on:  
Investigations of the Blood taken from Umbilical vein acc. to Profeta Law:-

→ Blood taken from umbilical vein → give -ve Serological tests

But this doesn't exclude syphilis  
Because the infant may develop it later on  
So → should be followed up During 3 months

→ Blood taken from Umbilical vein → +ve Result serological test

But this Doesn't mean that Baby is Syphilitic Because it may be D.t passive transfer of antibodies from the mother.

[C] More reliable test "Fluorescent treponema absorption" FTA test

using Fluorescein Labelled (IgM) that Doesn't cross the placenta → So will not give false +ve Results

[D] other test: repeated estimated of antibody titre.



# [A] Early Congenital Syphilis:

- Occur in: First 2 yrs
- Clinical manifest: = 2ry syphilis as it's a Blood Born Infection, No 1ry stage.
- The infant → may have the **Chancere** of the 1ry stage from a recently infected mother During Vaginal Delivery.

• The manifestation include:

## 1-Skin manifest:

- generalized Skin Rash. = Rash of 2ry stage.
- papular, papulosquamous, macular.
- Differ from stage 2 → it may be a bullous eruption specially on the palms - soles → That rupture to give Large raw Crusted area.
- mucous patches → affect the nasal mucosa giving rise to **Syphilitic rhinitis** → Difficult suckling
- Condyloma lata → similar to adult 2ry stage

## 2-Eye manifestations:

- Choroid oretinitis → manifest by: Salt and pepper fundus (on ophthalmoscopic exam)

## 3-CNS system:

- Syphilitic meningitis → bulging Fontanel's  
Hydrocephalus ↔ stiffness of the neck  
↔ Convulsions

## 4-CVS system: v. rare

## 5-Respiratory: Pneumonia → may be fatal

## 6-Liver-Spleen:

- Hepatosplenomegaly & liver cell failure
- Generalized lymphadenopathy

## 7-Kidney: → nephrotic syndrome → acute nephritis

## 8-Bone, Cartilage:

- \* First year affection: Syphilitic Osteochondritis in which there is inflammation in periosteum and Cartilage of epiphysis → painful Swelling of the epiphysis → limitation and loss of limb movements



- This is known as "Syphilitic Pseudoparalysis"
- The Radiological sign :- (Characteristic)

↳ Subperiosteal new bone formation → Giving the Bone the onion peel appearance

↳ Loss of density of the upper end of the tibia ~~is~~ "Wimberger Sign"

### \* 2nd year affection :

- Syphilitic Dactylitis → Inflammation in the periosteum and Bone of proximal phalanges

↓  
Leads to → painless Pusiform swelling of fingers

### ● Diagnosis :-

1. Clinical picture
2. Darkground microscopy for discharge of wet skin lesions
3. Radiological picture
4. Serological tests.

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## [B] Late Congenital Syphilis

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- Occur :- after the first 2 yrs
- Clinical manifestation :- Tertiary syphilis
- manifests by : Gumma in covering or supporting structure or viscero

### ● Manifestations [★] Hypersensitivity

1- Interstitial Keratitis :- → most common lesion

- It's a hypersensitivity reaction → Corneal Vascularization + Cellular infiltration
- On slit lamp :- the Vascularization appears Salmon Patches

The infiltrate appear :- ground glass.

- The condition Ends by :- Scar, opacity
- The tht → Steroids + antisyphilitic Drugs

2- Cochlear neuritis :-

- It's a Hypersensitivity reaction
- leads to → Inflammation of cochlear nerve + perceptive Deafness



- Conductive deafness → may occur as a complication of syphilitic Rhinitis in the early stage.

### 3 - Clutton arthritis

- It's a painless effusion in the joint
- Due to Hypersensitivity Reaction
  - affect mainly → Knee joint with little impairment of mobility.
- The Radiological finding → enlarged joint space • No Bone or Cartilage change.

### ★ 2 ★ Bone lesion

2 types of Bone affection

- ↳ First :- new bone formation → gives rise to parrot's nodes in the skull.
- ↳ Thick medial end of Clavicle → Higoumenakis sign
- ↳ Thick anterior Border of tibia  
Sabre tibia
- ↳ Second :- → Bone Destruction → gives Rise to Destruction of nasal septum

with collapse of the lower part of the nose and perforation of palate with food regurgitation

### ★ 3 ★ Neurosyphilis

leads to manifestations = aults.

### ★ 4 ★ CVS - Blood

- CVS affection → v. rare

- Blood affection → Paroxysmal Cold

Haemoglobinuria.

Feuer ★  
rigors  
Vikaria  
Jaundice  
Dark urine in exposure to cold

Caused by:

- presence of haemolysin that sensitizes the Red Blood cells in the presence of Complement During cold exposure.
- This haemolysin → Disappear on exposure to normal temperature.



# C Stigmata (Remainders) of Congenital Syphilis :-

- Permanent Scars + Deformation
- Result from → The early lesions of congenital Syphilis • Persist for life

## Stigmata of Early lesions

- 1 - Salt & pepper fundus
- 2 - Saddle nose :-
  - Result from → depressed nasal Bridge
  - D.t → Improper Development of nasal septum
- 3 - High arched palate :-
  - D.t improper development of Maxilla
- 4 - Bulldog face :-
  - Improper development of Maxilla renders the mandible more apparents
  - associated e.g. frontal bossing of the skull and saddle nose make bulldog face.
- 5 - Raghad's :-
  - linear scars at the angles of the mouth.

## Stigmata of Late Lesions

- 1 - Corneal opacity
- 2 - optic atrophy
- 3 - perceptive deafness
- 4 - Frontal bossing of the skull
- 5 - Sabre tibia

## 6 - Hutchinson teeth → Hutchinson triad :-

- upper Central incisors are small & widely separated and their sides converge towards the cutting edge → notch
- occur as a result of impaired tooth development

- interstitial Keratitis
- perceptive deafness
- Hutchinson teeth

## 7 - Moon's molars :-

- the first lower molar :- underdeveloped cusps with irregular surface.



# ⊞ Serological tests :-

## • Non-Specific tests :- of syphilis

- Demonstration of an antigen other than T. pallidum
- This antigen called: **Cardiolipin**  
[alcoholic extract of beef heart muscle]
- It has the ability to React with a gammaglobulin fraction of ptn's Serum called **Reagin**
- This Reagin → present in very small amounts in all normal sera. But in large amounts in the sera of syphilitic ptns to the Degree of reacting with the antigen Cardiolipin
- to produce → Visible Reaction either through → Flocculation OR Complement fixation Reaction.
- The other name of those Tests :-
  - non-treponemal tests
  - Reagin test

## \* the advantages of these tests :-

- Cheap and easy to performed
- good screening tests
- They become -ve after the effective the so
- They can be used in Follow up of ptns under treatment specially if quantitative estimation of their titre is performed

## \* The Disadvantages of Tests :-

- give Both false +ve and false -ve results so they have to be Confirmed w one of the specific treponemal test.

## ★ False +ve Results: Due to :-

- 1- technical faults in samples collection or reagents
- 2- Physiological conditions in pregnancy.
- 3- Old age.
- 4- Pathological conditions in which there is liberation of the antigen **Cardiolipin** from Organisms other than the treponema.  
OR from the mitochondria of the cells in Diseases with tissue Destruction



- Examples :- of acute condition that give False +ve Results

- ↳ Viral pneumonia    ↳ malaria
- ↳ Hepatitis            ↳ measles
- ↳ chickenpox          ↳ vaccination
- ↳ Treponemal Diseases other than syphilis

- Examples of Chronic conditions with False +ve Results:-

- ↳ Lupus Erythematosus    ↳ RA    ↳ anemia
- ↳ leprosy    ↳ malignancy

★ False -ve Results:- Due to Prozone phenomenon → in which the High Concentration of antibodies in the ptn serum may not give the Flocculation reaction except after its Dilution to a particular Low Concentration.

- Those Serial Dilutions of ptn serum used to avoid false -ve Results:-

1. Flocculation tests
2. Complement fixation tests

## II Flocculation tests :-

• The Purified Cardiolipin antigen Mixed with small amounts of syphilitic serum ⇒ Causes Flocculation that can be detected By:- the naked eye or microscope.

• Examples of these tests

① ↳ Veneral Disease research Laboratory (VDRL)

② ↳ Rapid plasma Antigen (RPR) :- done by mixing Carbon containing Cardiolipin antigen suspension with ptn serum on a disposable Test Card with rotation for 8 minutes

- flocculation of Carbon particles visible to naked eye.

• Both tests are good Screening tests and can be quantitated to assess the progress of the Disease in follow up

## ② Complement Fixation test

Wasserman Reaction (WR)



- In this test the Cardiolipin (antigen) is used which in the presence of the (antibody) in the ptn serum will bind the (Complement)

- In the 2nd step an (Indicator System) formed of Sensitized sheep red cells added

- If the ptn is Syphilitic the Complement is Consumed in the first step → preventing haemolysis of Red cells in the 2nd step.

- many Labs Don't use this test as flocculation tests → easier to perform  
→ cheaper  
→ equally efficient

## 1. Specific Tests :-

- Specific as they depends on: Demonstration of treponemal antigen

- So they called Treponemal Tests:

### ★ Advantages:

- accurate in the Diagnosis
- Don't give False Results
- They performed to Confirm the Results of non-specific test

### ★ the Disadvantages:

- expensive
- technically difficult
- they Remain +ve even after the effective antisyphilitic ~~the~~
- they Can't be used in follow-up of ptn.

## 1. Treponema pallidum haemagglutination

- Relatively simple & less expensive Test
- The antigen → is the Sensitized sheep RBCs that are Coated w/ treponemal antigen added to ptn serum in one test tube
- in other test tube :- the non-sensitized sheep RBCs are added to another sample of ptn's serum [considered the **Control tube**]
- Test considered +ve → when there is visible agglutination of RBCs in the first tube  
↓  
Button shaped D.t presence of antibodies in ptn's serum
- The Control Tube → will Not show this Agglutination



Because of its simplicity and lack of need for microscopic examination and Lab. facilities

- It's the most widely using test in Developing Countries including Egypt

## 2) Treponema pallidum immobilization

- The Antigen is the virulent Treponema
- Nichol strain obtained from the infected rabbit added to the ptn Serum in the PR Complement
- If ptn is syphilitic → The antibodies in his serum will inhibit the motility of Treponema
- This test is Technically Difficult
- needs microscopic examination.

## 3) Fluorescent treponema Antibody Test

- The Antigen is :- Suspension of dead Treponema pallidum (Nichol strain) That is placed on the slide together with the ptn serum.

- Syphilitic antibodies if present in the a2 Serum → will coat the Treponema

- To test for this union → Fluorescein labelled antihuman globulin (Conjugate) is added.

→ If the syphilitic antibody has coated the Treponema → The conjugate reacts with them → producing :- fluorescence when viewed under the ultra-violet microscope

## 4) Fluorescent treponemal antibody absorption Test

- The ptn's Serum is diluted at first with a Culture extract of other Treponema to absorb the non-specific antibodies of other Treponemas.

- The Rest of the Test → is performed as previous.

- This modification → will avoid false +ve results of the test Due to other Treponema



- The Advantages of this test :-
  - ↳ the only +ve test in the early phase of 1ry syphilis.
  - ↳ the test can be made more specific by the use of **specific** class of fluorescein labelled antihuman globulin against human (IgM)
- Since IgM antibodies can't cross the placenta → a reactive test in the infant specifically indicates: Congenital syphilis infection.
- the frequent determination of the titers using the non-treponemal Test in the infant is :-
  - ↳ less expensive
  - ↳ more easy to be performed
- They are the standard tests in the Diagnosis of Congenital syphilis in infants

## 5) Reiter protein Complement Fixation Test

- The Antigen is :- the protein derived from Reiter strain of treponema that is Antigenically similar to T. pallidum
- Its added to the pt's Serum with a Complement
- Its Not in common use as other previous tests

## ± Treatment of Syphilis.

### ① → Basic principles :-

- 1 - The Drug of choice for the treatment of syphilis is penicillin
- 2 - The treponema → Can reach any Organ in Body including: CNS in 40%.
  - ↳ This Require Antibiotic that passes BBB
- 3 - The average doubling time of Treponema is over 30 hrs → which requires a treponemicidal level in the invaded tissue for at least 8 days.
  - They are also affected by Low levels of Penicillins in Blood that are (0.03 unit/ml)



4 - Because of CNS → invasion in 40% of pts and the inability of the Long-acting Benzathine penicillin to pass BBB

The Drug of choice is → Procaine Penicillin daily injection for 10 days

## ② ⇒ Treatment of Early Stage :-

one of the following regimens can be used in the early stage within the first 2 yrs of infections:-

1- procaine penicillin (600,000) units I.M daily for 10 days (total dose 6 million Unit)

2 - Long acting Benzathine penicillin 2.4 million units → I.M in One single injection.

• although this single long-acting Benzathine penicillin is Better than the repeated procaine penicillin injections as regards the ptn compliance to treatment

• The procaine penicillin is Better used to save about 40% of CNS complications

## ③ ⇒ Treatment of Late Stage

one of these Regimens → used in Late stages after 2 yrs of infection:-

1 - procaine penicillin (600,000) unit - I.M daily for 20 Days (total 12 million units)

2 - Long acting Benzathine penicillin 3 million units I.M → every week for 4 weeks (total 12 million units)

## ④ ⇒ Treatment of CVS Syphilis

the same of late stage is used in addition to specific ~~ttt~~ of Heart failure or aneurysm

## ⑤ ⇒ Treatment of Neurosyphilis :-

• The Long acting penicillin → Not effective in this condition as its Lipid insoluble + Have Very Low penetration of BBB

• The Following Regimen → Can used in Order to achieve Treponemicidal levels in the CSF :-